SCIENTIFIC LETTER

Haemodynamic significance of stent lesions compared to native coronary lesions: a myocardial perfusion imaging study

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The relation between the angiographic severity of a coronary lesion and its functional significance has been studied extensively for native coronary lesions.[1] Diameter stenosis, lesion length, lesion eccentricity, and lesion complexity have been found in both in vitro and in vivo studies to determine the haemodynamic relevance of a coronary lesion.[2 3] In a recent meta-analysis, nearly 60% of patients with a > 50% diameter stenosis in a restenotic stent were found to be asymptomatic.[4] Stent restenosis differs from native coronary lesions in its morphology, histology, and geometry.[5] Usually the stent structure, which is either round or oval, is covered by a relatively smooth neointimal layer. Thus, in contrast to native coronary lesions, which may have an eccentric and complex cross sectional geometry, the lumen of a stent restenosis is thought to have a more homogenous and less complex geometry. Therefore, the lesion severity threshold for limiting coronary flow reserve may be higher in stent restenoses than in native lesions. To test this hypothesis, we performed a direct comparison between stent and native lesions regarding their haemodynamic relevance.

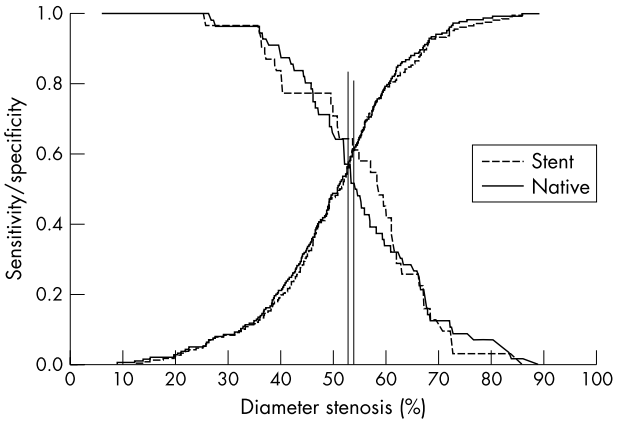

Figure 1 Relation between sensitivity and specificity of diameter stenosis for prediction of a reversible perfusion defect. Dotted lines represent stent lesions; solid lines represent native lesions; solid vertical lines indicate thresholds where sensitivity equals specificity; n = 242.

METHODS

Patients were identified from our angiography and myocardial perfusion imaging databases by a computerised search. They included 14 399 coronary angiographies in the angiographic database and 4644 stress perfusion studies in the myocardial perfusion imaging database, collected between 1998–2001. Patients had to have undergone myocardial perfusion imaging within two months of coronary angiography to determine the haemodynamic impact of a single coronary lesion assessed as potentially flow limiting by angiography. The lesion had to be either a native coronary lesion or a stent restenosis. Exclusion criteria were: acute coronary syndromes or coronary revascularisation in the period between diagnostic angiography and nuclear imaging; the presence of more than one potentially flow limiting lesion; prior bypass surgery; valvar heart disease; complete occlusion of the target vessel; side branch involvement; and wall motion abnormalities on cine ventriculography. Finally, 93 patients with a stent restenosis in a native coronary vessel and 149 patients with a native coronary lesion were identified.

Digitised coronary angiograms were analysed off-line using a computer assisted, automated, edge detection system. Angiograms were analysed without knowledge of nuclear or clinical data.

Myocardial perfusion imaging was performed using Tc-99m sestamibi SPECT. Anti-anginal medications were discontinued on the day of the stress test and β blockers were discontinued two days before the stress test. In patients who were unable to exercise, a pharmacological stress test was performed using 0.56 mg/kg dipyridamole. The images were analysed both visually and semi-quantitatively by two experienced nuclear cardiologists who were blinded to the results of quantitative coronary angiography. A coronary lesion was defined as haemodynamically relevant if there was a reversible perfusion defect in the distribution territory of the target vessel.

RESULTS

Diameter stenosis was between 40% and 70% in 179/242 (74%) of lesions. Mean (SD) reference diameter (2.67 (0.52) mm *v* 2.7 (0.62) mm), diameter stenosis (50 (14%) *v* 51 (14%)), lesion length (10.4 (5.1) mm *v* 10.5 (4.6) mm), parameters of perfusion imaging, and incidence of perfusion defects were similar for the stent and native lesion groups. In the stent group there were more patients either with a history of, or ECG findings of, prior myocardial infarction in the target vessel territory (33% *v* 17%, p = 0.01) and more patients with a lesion in the right coronary artery (34% *v* 20%, p = 0.02) than in the native group.

Sensitivity and specificity curves were constructed for diameter stenosis to predict a haemodynamically relevant lesion. The diameter stenosis at the intersection point of sensitivity and specificity curves was determined (fig 1). Diameter stenosis at the intersection point was 53% for stent lesions and 53% for native lesions. Receiver operator curves yielded similar values for the areas under the curve (stent group 0.63, 95% confidence interval (CI) 0.52 to 0.74 *v* native group 0.61, 95% CI 0.52 to 0.70, respectively). The intersection points of sensitivity and specificity to detect a haemodynamically significant stenosis were 62% for stent lesions versus 57% for native lesions. Results were not

different when patients with prior myocardial infarction were excluded from the analysis.

Univariate predictors for a reversible perfusion defect were: prior myocardial infarction (odds ratio (OR) 2.16, $p = 0.01$); diameter stenosis (OR 1.04, $p < 0.01$); minimal lumen diameter (OR 0.27, $p < 0.01$); a resting perfusion defect (OR 2.98, $p < 0.01$) and angina during stress perfusion imaging (OR 2.19, $p = 0.04$). Multivariate predictors for a reversible perfusion defect were diameter stenosis (OR 1.05, $p < 0.01$) and a resting perfusion defect (OR 2.38, $p = 0.04$).

DISCUSSION

The major findings of this study are threefold; firstly, the threshold diameter stenosis of coronary lesions for reversible perfusion defects during stress myocardial perfusion scintigraphy is similar for stent restenoses and native coronary lesions. Secondly, lesion type, both native and stent restenotic, is not a predictor of haemodynamic significance. Thirdly, diagnostic accuracy of angiographic variables to assess the haemodynamic significance of intermediate lesions is low in both stent and native lesions.

In a study using dipyridamole stress echocardiography, complex coronary lesion morphology has been found to be more frequently associated with pathological findings than simple coronary lesions despite similar diameter stenoses indicating the importance of lesion complexity on functional significance.[3] In contrast to native coronary lesions which may have an eccentric cross sectional geometry, the lumen of stent restenosis is thought to have a more homogenous and less complex lumen geometry. The consequence should be less resistance to flow; however, the results of this study do not support the hypothesis that stent restenosis requires a higher angiographic diameter stenosis than native coronary lesions to result in reversible perfusion defects. We have shown that angiographic assessment does not systemically overestimate or underestimate the functional severity of a stent lesion as compared to a native coronary lesion. This was demonstrated in a relatively large number of patients with balanced baseline characteristics for both groups.

An important, but not unexpected, finding is the low diagnostic accuracy of quantitative angiography to predict the functional significance of intermediate lesions in both native and stent lesions. Considering these data, a decision to revascularise an intermediate stent restenosis in an asymptomatic patient should be based on non-invasive imaging or on functional invasive methods (for example, fractional flow reserve) to assess the functional severity of stent restenosis. When the data of Ruygrok and colleagues are viewed in the light of the low predictive accuracy of angiography to predict the haemodynamic relevance of a lesion, it is not surprising that 58% of patients with angiographic stent restenosis were asymptomatic.[4] The absence of symptoms is not explained by a more benign haemodynamic impact of stent lesions as compared with native lesions but by the low predictive value of angiographic diameter stenosis for haemodynamic and clinical relevance of a stenosis.

Several limitations of the study have to be recognised. Firstly, it is a retrospective study. Secondly, myocardial perfusion imaging has its limitations, such as attenuation artefacts, that may partially explain the lack of correlation with angiography. Thirdly, it might be argued that this study was underpowered to show a significant difference in the haemodynamic impact of stent lesions as compared to native lesions. However, there was no trend towards a different haemodynamic relevance of stent restenosis, suggesting that significantly greater patient numbers were unlikely to have resulted in a different outcome.

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